MICROSTIMULATORS AND MICROTRANSDUCERS FOR FUNCTIONAL NEUROMUSCULAR STIMULATION

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ALFRED E. MANN FOUNDATION FOR SCIENTIFIC RESEARCH
12744 San Fernando Road, Sylmar, CA 91342
Joseph H. Schulman, Ph.D., Principal Investigator
John Gord, David Payne, Abe Smith, Cecilia Tanacs

BIO-MEDICAL ENGINEERING UNIT, QUEEN'S UNIVERSITY
Kingston, ON K7L 3N6 CANADA
Frances J.R. Richmond, Ph.D., Principal Investigator
Gerald Loeb, Kevin Hood, Ray Peck, Anne Dupont, Tiina Liinamaa

PRITZKER INSTITUTE OF MEDICAL ENGINEERING, ILLINOIS INSTITUTE OF TECHNOLOGY
Philip R. Troyk, Ph.D., Principal Investigator

Abstract

We are developing a new class of implantable electronic devices for a wide range of neural prosthetic applications. Each implant consists of a microminiature capsule that can be injected into any desired location through a 12 gauge hypodermic needle. Multiple implants receive power and digitally-encoded command signals from an RF field established by a single external coil. The first type of implant is a single-channel microstimulator equipped with capacitor-electrodes that store charge electrolytically and release it upon command as current-regulated stimulation pulses. We are also working on implants equipped with bidirectional telemetry that can be used to record sensory feedback or motor command signals and transmit them to the external control system.

In the past quarter, we finalized implant materials and began preclinical regulatory testing of these materials in preparation for clinical trials. New production jigs have been built to support the improved assembly and sealing methods and the first working, hermetic microstimulators built with these materials and jigs have been delivered for long-term testing. New transmitter circuits and coils have been built for bench tests, chronic animal stimulation, and clinical beta testing. They are being interfaced with nine prototype bedside controllers equipped with an improved dry test well and operated by our new PC-Windows™ software. We have prepared a journal article quantifying the ability of our microstimulators to produce graded and regional recruitment of muscle.

Redesign and relayout of the 2 MHz version of the microstim chip was performed to obtain a 20 volt compliance, and other improvements. The repeater test chip and other test patterns were redesigned and relayed out. A design review was held for these designs and several improvements were suggested.

Implantable Devices

Seals

The first working devices based on the new hermetic sealing techniques were produced at AEMF and are in testing at Queen's University. We are now using the same glass for both feedthrough beads and the capsule tubing. Residual stress in the glass was measured as acceptable, in fact well below critical values, and there were no detectable leaks at the measurement limit of 1×10^{-10} cc atm He/sec. Improved fixtures and laser controls are starting to yield good quality hermetic seals.

Electrochemistry

We have modified the electrochemical procedures for preparing the electrodes as described in detail in our last QPR. In particular, we have discovered that the sintered tantalum electrode anodizes much quicker (4 vs. 24 hours) and produces lower leakage current (<0.1 vs. <1.0 μA) when we use 1.0vol% phosphoric acid instead of the 0.1%

acid that was recommended to us. The lower concentration was probably more appropriate for relatively small and coarse Ta surfaces. Our relatively large Ta slug and its deep and finely porous structure tended to produce excessive electrolysis of the water with the low ionic content solution. Much more of the applied current of 500 μA seems to go to anodizing the Ta with the 1% acid.

We have also simplified manufacturing by omitting the activation of the Ir electrode by cyclic voltammetry, which required a complex and tedious sequence of steps that would have been awkward for assembly technicians. We do not expect this to have any measurable effect on microstimulator function for the following reasons:

- Ir already appears to be somewhat activated, probably as a result of oxide formation during welding and sealing and will probably continue to activate somewhat with prolonged pulsing if intense enough to approach electrolysis limits;
- total impedance of load is dominated by tissue rather than metal/electrolyte interface;
- maximal charge density is safe even for unactivated Ir or Pt (32 mA x 0.25 ms = 8 $\mu C/4.7mm^2$ = 170 $\mu C/cm^2$ < 300 $\mu C/cm^2$ generally accepted safe limit).

Spring Contact

We wish to eliminate the loose stainless steel spring and its mechanical-electrical contact to the Pt-Ir feedthrough tube via the welded Pt-Ir washer. We have obtained supplies of conical springs made from three different alloys that should be able to resist any heat that may be transmitted through the glass bead to the Pt-Ir tube during the final glass-to-glass seal with the capillary. The small end of these springs fits snugly on the Pt-

Ir tube and we have successfully YAG laser welded all three spring types directly to this tube. Pull-strength and cross-sectional tests and gold plating trials are underway. The large end of the conical shape will be accommodated by our new PC-board design, which will be released as soon as the new ASIC is released to the foundry.

- ***RF Coupling to Electronic Subassemblies***

Previous builds of the electronic subassemblies for the microstimulator had inconsistent and undesirably narrow tolerance to RF field strength and/or modulation depth. These problems were supposed to have been corrected by the repairs to the Orbit ASIC and the addition of the external discrete diode and resistor, but may have resurfaced due to poor control of the fabrication of the electronic subassembly, which includes several critical parts placement, wire bonding, and coil winding steps. New tests confirm this hypothesis. Recently built subassemblies had much broader and more consistent tolerance to field strength and were able to detect very weak modulation reliably, as shown in the accompanying table. Further improvements are underway and will be evaluated similarly. We are now measuring the practical consequences of these improvements on completed devices in terms of the ability to provide reliable control and power when microstimulators are located at a distance from the transmission coil or oriented out of alignment with its magnetic flux lines.

FIELD STRENGTH AND MODULATION TEST

No.	Addr	Rcvr. Coil Freq. (MHz)	Transmitter Coil Current		Modulation Depth @ 1.0 A Coil Current	
			MIN.	MAX	MIN.	MAX.
1	085	1.90	600ma	5.8 A	96.2% /100%	< 80% /100%
2	001	1.93	780ma	4.0A	93.6% / 100%	< 80% /100%
3	255	2.00	400ma	7.3A	97.8% / 100%	< 80% /100%
4	003	1.95	320ma	6.4A	97.8% / 100%	< 80% /100%
5	015	NT	800ma	6.0A	97.8% / 100%	< 80% /100%
6	085	NT	800ma	6.8A	96.5% / 100%	< 80% /100%
7	001	NT	640ma	>8 A	NT	NT

NOTE: ALL TESTS WERE DONE WHILE THE CHIP1 WAS UNDERGOING A PULSE WIDTH RAMP TEST.

NOTE: THE FIRST FOUR UNITS WERE THE COMPLETED UNITS, AND THE NEXT THREE WERE WOUND ELECTRONIC ASSEMBLIES.

External Equipment

Bedside Controllers

The first batch of 9 bedside controller prototypes is being fitted with new coils and drivers for various fixed configurations needed for preclinical testing. These include two large coils for placing around cats (received and installed), one shoulder pad to test concepts for the subluxation trial (designed and under construction), and five hand held coils for beta testing of the clinician's software package (prototype of new design built). These bedside controllers all incorporate a relatively large PCB containing coil driving circuitry that is specific to a given transmission coil. We are working on a redesign of the coil drivers in which the driver circuitry is sufficiently small that it can be located outside the bedside controller and close to or even on the transmitting coil. These coil/driver units would then be interchangeable so that any given bedside controller can operate with a hand held coil for the clinician's drywell testing and threshold measurements or with various wearable coils for patient use.

Test well Accessories

A new drywell tester for use prior to implantation has been designed. It incorporates a preamplifier module in the drywell connector, which provides interchangeability with the wetwell tester used to quantify the stimulus output of the implants. The new drywell uses computer-aided machining to improve manufacturability by incorporating into one Plexiglas component all complex contours required for locating

the device to be tested, positioning sensing electrodes, and providing strain relief for the attached cable.

Software

All user interfaces and control functions of the new Clinician's Fitting software have been implemented and tested successfully. A complete Users Manual is appended. Remaining work includes further development of clinical report writing features (to be designed in consultation with clinicians during beta test) and systematic failure-mode analysis and quality assurance testing for regulatory requirements.

Preclinical Regulatory Testing

The first batch of implant materials has been sent to a contract biocompatibility house for required in vitro testing, including mutagenicity (Ames Test, Sister Chromatid Exchange Test, and Chromosomal Aberration Test), intracutaneous toxicity sensitization, systemic toxicity and cytotoxicity. Additional dummy devices are under construction to complete these in vitro tests and to serve as passive controls for the next phase of chronic animal testing. The first stage of device characterization and chronic animal testing has been summarized in four journal articles listed below (two in press, two submitted).

Administrative

Rather voluminous documentation on all phases of the internal and external devices and accessories is required for regulatory approval of system design, quality assurance procedures, material specifications, manufacturing and testing procedures, etc. Queen's University was visited by the quality assurance consultant for Advanced Bionics Corp., who conducted a Good Laboratory Practices (GLP) audit of our facilities and advised us on structuring the documentation and document control system required for Good Manufacturing Practices (GMP) of the U.S. Food and Drug Administration. The required documentation appears to be about 50% complete at this time.

After encountering some potential conflicts with the use of the proposed MicroStim trademark, it has been decided to use the trademark BION™, signifying a bionic neuron, which could apply equally well to the motor stimulation devices now available as well as the sensor and outgoing telemetry system now under development for functional neuromuscular stimulation.

Integrated Circuit Development

The 2 MHz μstim I.C. chip relayout was completed for the new foundry. This new chip is capable of functioning in both polarities at 20 volts. The repeater chip layout was improved and a major design review was held at AEMF, with major analog circuits experts from Advanced Bionics, Pacesetter Systems, and Alfred E. Mann Foundation present. Eight problem areas were discovered and subsequently corrected. The repeater

chip, i.e., layout, is presently being completed. The foundry that we will be using has been successfully making other chips for AEMF. The foundry has worked closely with us on this high voltage I.C. design. A major design review is being planned for late October or early November.

Plans for Next Quarter

We anticipate completing all preclinical regulatory testing by January and will submit the documentation to the Canadian Health Protection Branch for approval of the system for shoulder subluxation trial at Queen's University (institutional approval of the protocol was obtained previously, pending HPB approval). Similar documentation will be used for a U.S. FDA application for Investigational Device Exemption (IDE) to permit multicenter trials. Approvals of the same system for treatment of urinary stress incontinence will be sought as soon as the first clinical experience with the shoulder implants has been obtained; the initial trials will be in Toronto. (This effort is supported by Advanced Bionics Corp., the Ontario Rehabilitation Technology Consortium and the Canadian Neuroscience Network of Centres of Excellence and the Foundation is giving additional support over and above the financing from the NIH.

We will redesign the 2 MHz Class E coil driver to reduce its size and improve its power efficiency and manufacturability in preparation for clinical trials.

We expect to complete the layout of the repeater chip and have the foundry make the chips. When the chips come from the foundry we expect to evaluate on the bench these new ASICs for both the microstimulator and the repeater. This should permit us to

complete the specification of the bidirectional suspended carrier transmission scheme, which is the key to the microtransducer and telemetry system.

Status of Refereed Journal Articles

Cameron, T, GE Loeb, RA Peck, JH Schulman, P Strojnik and PR Troyk. Micromodular implants to provide electrical stimulation of paralyzed muscles and limbs. IEEE Trans. Biomed. Engng., in press.

Fitzpatrick, TL, TL Liinamaa, I Brown, T Cameron and FJR Richmond. A novel method to identify migration of small implantable devices. J. Long-Term Effects of Medical Implants, in press.

Cameron, T, FJR Richmond and GE Loeb. Effects of regional stimulation using a miniature stimulator implanted in feline posterior biceps femoris. IEEE Trans. Biomed. Engng., submitted and appended to this QPR.

Cameron, T, TL Liinamaa, GE Loeb and FJR Richmond Long-term biocompatibility of a miniature stimulator implanted in feline hind limb muscles, in preparation, to be included in next QPR.

List of Appended Material

Cameron et al., Effects of Regional Stimulation...

ClinFit Users Manual